

Varelisa® Sm Antibodies - Device Modification
510(k) Submission
Section 9. Summary of Safety and Effectiveness

510(K) SUMMARY OF SAFETY AND EFFECTIVENESS

This summary of safety and effectiveness information is being submitted in accordance with the requirements of The Safety Medical Devices Act of 1990 (SMDA 1990) and 21 CFR Part 807.92.

Assigned 510(k) Number: K000312

Date of Summary Preparation: January 20, 2000

Distributor: Pharmacia & Upjohn
Diagnostics Division, US Operation
7425-248-1
7000 Portage Road
Kalamazoo, MI 49001

Manufacturer: Pharmacia & Upjohn Diagnostics GmbH Co. KG
Munzingerstrasse 7
D-79111 Freiburg, Germany

Company Contact Person: Karen E.Matis
Manager, Regulatory Affairs and Quality
Management
Diagnostics Division
US Operation
7000 Portage Road
7425-248-01
Kalamazoo, MI 49001
(614) 794-3324 (Phone)
(614) 794-0266 (Fax)

Device Name: Varelisa® Sm Antibodies

Common Name: Antinuclear antibody immunological test

Classification:

<u>Product Name</u>	<u>Product Code</u>	<u>Class</u>	<u>CFR</u>
Varelisa® Sm Antibodies	82 LKP	II	866.5100

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Substantial Equivalence to:

Varelisa® Sm Antibodies (previous version, as cleared by FDA)

Intended Use Statement:

The Varelisa Sm Antibodies EIA kit is designed for the semiquantitative and qualitative determination of Sm antibodies in serum or plasma to aid in the diagnosis of Systemic Lupus Erythematosus (SLE).

General Description of the Device

The Varelisa Sm Antibodies is an enzyme immunoassay for the semiquantitative and qualitative determination of Sm antibodies in serum or plasma.

A characteristic feature of many rheumatic diseases is the presence of circulating antinuclear antibodies. The anti-Sm antibody is regarded as a pathognomonic marker for Systemic Lupus Erythematosus (SLE).¹ The presence of autoantibodies to Sm is one criterion for SLE as defined by the American Rheumatism Association (ARA).

The Sm proteins form a common core in each snRNP particle involved in splicing. The core is composed of eight small polypeptides, designated B, B', D1, D2, D3, E, F and G, that range in size from 10 to 29 kDa. The major targets in autoimmune diseases are the B and D polypeptides.² Both polypeptides are contained in the antigen preparation used in the Varelisa Sm Antibodies Assay.

¹ Craft, J. (1992); Antibodies to snRNPs in systemic lupus erythematosus; *Rheum.Dis.Clin.North Am.* 18, 311-335

² Peng, S.L., Craft, J.E. (1996); Spliceosomal snRNPs Autoantibodies; In: J.B. Peter & Y. Shoenfeld (Eds.), *Autoantibodies*, pp. 774-782, Elsevier Science B.B., Amsterdam

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Varelisa® Sm Antibodies Test Principle

Varelisa Sm Antibodies is an indirect noncompetitive enzyme immunoassay. The wells of a microplate are coated with purified Sm antigen. Antibodies specific for Sm present in a patient sample bind to this antigen.

In a second step an enzyme labeled second antibody (Conjugate) binds to the antigen-antibody complex which leads to the formation of an enzyme labeled antigen-antibody sandwich complex.

The enzyme labeled antigen-antibody complex converts the added substrate to form a colored solution. The rate of color formation from the chromogen is a function of the amount of Conjugate complexed with the bound antibody and thus is proportional to the initial concentration of the respective antibodies in the patient sample.

Device Comparison:

Both old and new versions of the Varelisa® Sm Antibodies Assay, are indirect noncompetitive enzyme immunoassays for the determination of Sm antibodies in serum or plasma, which share many common features.

The essential difference between both assays is the use of internally produced Sm antigen purified from calf thymus by Ion Exchange Chromatography instead of affinity-purified material from an external supplier, spiked with Sm BB' proteins. The antigen preparation of the new version still contains the major antigenic components, SmD and SmBB', which ensures a similar specificity.

In addition, the disease area in the intended use was restricted to systemic lupus erythematosus (SLE). Mixed connective tissue disease (MCTD) is no longer included because according to recent literature, antibodies against Sm are regarded indicative for SLE more than for MCTD.

Laboratory Equivalence

In the correlation study a high degree of similarity is demonstrated when comparing 47 samples tested in both assays:

From the regression analysis, a correlation coefficient of $R^2 = 0.803$ (Pearson's coefficient of correlation $r = 0.896$) was obtained. Intercept and slope are reasonably close to 0 and 1 respectively.

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Omitting 8 samples (out of 47 samples) which were found equivocal in the new Varelista Sm Antibodies Assay, the overall agreement was 95 % (37 / 39 samples). These samples were excluded, because for the old version of the assay, no equivocal range was defined.

All negative samples (blood donors) were found negative in both assays.

The few differing results are probably due to the different antigen composition caused by the different purification methods.

This study clearly demonstrates that the new and the old version of the Varelista Sm Antibodies Assay are substantially equivalent.



DEPARTMENT OF HEALTH & HUMAN SERVICES

MAR 17 2000

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Ms. Karen E. Matis
Manager, Regulatory Affairs and Quality Management
Pharmacia & Upjohn
Diagnostics Division, US Operations
5094 St. Andrews Drive
Westerville, Ohio 43082

Re: K000312
Trade Name: Varelisa® Sm Antibodies
Regulatory Class: II
Product Code: LKP
Dated: January 28, 2000
Received: February 1, 2000

Dear Ms. Matis:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

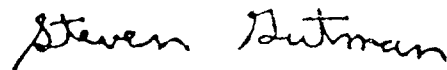
If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

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This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsma/dsmamain.html>".

Sincerely yours,

A handwritten signature in black ink that reads "Steven Gutman". The signature is written in a cursive, flowing style.

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

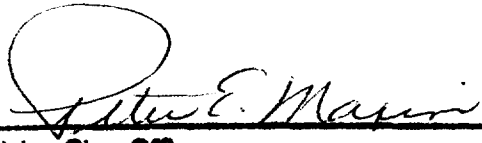
Enclosure

Varelisa® Sm Antibodies- Device Modification
510(k) Submission
Section 1. Indications For Use Statement

510(k) Number: K000312

Device Name: **Varelisa® Sm Antibodies**

The Varelisa Sm Antibodies EIA kit is designed for the semiquantitative and qualitative determination of Sm antibodies in serum or plasma to aid in the diagnosis of Systemic Lupus Erythematosus (SLE).


(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K000312

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE
IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓

OR

Over-The-Counter Use _____

(Per 21 CFR 801.109)